

Letter to the Editor

In Response to *Distinct Histopathology Characteristics in Empty Nose Syndrome*

In Reply:

We thank Dr. Salzano for their interest in our article¹ and the chance to have an inspiring discussion about empty nose syndrome (ENS). We concur in the importance of microbiota on nasal inflammation in many kinds of sinonasal dysfunctions; nevertheless, we have some different considerations regarding Dr. Salzano's opinions.

First, although certain enrollees had a nasal allergy in our study, the histological changes of ENS and allergic rhinitis are quite distinct from each other. The histopathology of allergic rhinitis is characterized by abundant submucosal glands, increased venous sinusoids, and edema of lamina propria with limited fibrotic change.² The biopsied tissue from atopic subjects in this study still revealed prominent submucosal fibrosis with glandular atrophy, indicating a substantial tissue remodeling similar to atrophic rhinitis.¹ We considered the impact of allergic rhinitis on ENS is noteworthy but unidentified.

Second, we agreed that nasal microbiota plays an important role in neuroimmune inflammation and epithelial barrier functions; however, the clinical experience showed that infections of the sinonasal cavity were mostly lacking in ENS.^{3,4} The nasal dysbiosis may not be evident in this disease entity and thus we did not investigate as main objective. The relationship between nasal dysbiosis and ENS need further study to clarify.

Third, in the discussion section of the retrospective study,⁵ the authors addressed that patients with tumor and inflammatory disease may have different perspective on function. Therefore, such functional outcome analysis in tumor patients may not be appropriate to apply on inflammatory sinonasal sufferers. Besides, this study did not use questionnaires specifically regarding ENS like ENS6Q or SNOT-25 and might underestimate the symptoms related to ENS.

Fourth, computational fluid dynamic (CFD) analysis in ENS has shown a reduced airflow and wall shear

stress around inferior turbinate, which has a negative correlation with symptom scores.⁶ The CFD study revealed that air-mucosal stimulation is crucial in these patients. We found an underexpression rather than negative expression of TRPM8 in patients with ENS, so it's possible that lateral wall implantation can improve airflow pattern and wall shear stress and then improve the associated symptoms subsequently.

Finally, the pathophysiology of ENS remained a puzzle to us and, as what you said, that the factors responsible for ENS are manifold. Researches focus on nasal microenvironment and mucosal firewall in ENS should be developed in the future. We hope our study will shed some light in this complex disease and help in patient-centered care for rhinologists around the world.

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The authors have no funding, financial relationships, or conflicts of interest to disclose.

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